THE EFFECT OF CHRONIC HYPERCAPNIA ON OXYGEN AFFINITY AND 2, 3 DIPHOSPHOGLYCERATE AS RELATED TO SUBMARINE EXPOSURE

by

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THE PROBLEM

To better define the pH controlled regulation of oxygen re-

affect 2,3 DPG levels, follow the pH changes with a time lag.

In vitro the pH dependent changes in 2,3 DPG take place within three hours under optimal conditions[16].

In adaptation to high altitude, a fall in pH due to hypocapnia of hyperventilation occurs together with hypoxia resulting in a simultaneous rise in 2,3 DPG and P_{50}.

Evidence indicating that the rise in pH contributes to the increase in 2,3 DPG in hypoxia has been provided by Gerlach et al.[17] who demonstrated that the increase in 2,3 DPG produced by 24-hour exposure of rats to 11% O_2 was abolished when 5% CO_2 was added to the low oxygen gas mixture. In human subject, studied at high altitude, the 2,3 DPG changes reached one-half of its maximum within six hours and the maximum within 24 hours after arriving at altitude[18]. Although the 2,3 DPG changes in chronic hypercapnia are in opposite direction, the time sequence reported here is similar to that observed in altitude adaptation.

While the decrease of 2,3 DPG follows the fall in pH with a time lag during the uncompensated phase of respiratory acidosis, the subsequent increase in 2,3 DPG during the compensated phase of respiratory acidosis (three and seven days) does not exhibit a time lag but closely parallels the rise in pH. This difference in the relationship of pH here demonstrate clearly that the red cell pH changes are the primary cause of the changes in oxygen affinity.

We have demonstrated in chronic hypercapnia the involvement of two mechanisms, which are pH dependent and are known to influence oxygen affinity: 1) changes in 2,3 DPG, and 2) changes in red cell cations[2]. The latter findings were obtained in previous work carried out under identical experimental conditions. The correlation coefficients between P_{50} and 2,3 DPG were 0.93 and between P_{50} and red cell cations 0.97. There is obviously a relation between 2,3 DPG changes and red cell cation permeability in chronic hypercapnia. It is not possible to state, at this time, how they are linked together.

The observed findings on 2,3 DPG changes in chronic hypercapnia underline the significance of the pH controlled regulation of oxygen release from hemoglobin which has recently been emphasized by Astrup[19] on the basis of clinical studies.

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The relationship between oxygen affinity and 2, 3 diphosphoglycerate (2,3 DPG) in the red cell has been studied in chronic hypercapnia induced by prolonged exposure of guinea pigs to 15% CO_2 in 21% O_2. Red cell pH fell to a minimum after six hours of exposure and subsequently rose without reaching initial values after seven days of exposure. Both oxygen half-saturation pressure (P_{50}) and the level of 2, 3 DPG of the red cells followed the time course of the pH changes. However, both parameters required 24 hours to reach a minimum, following which they increased steadily and were not different from control values after seven days of exposure.

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